

APPENDIX A

VERSION OF SPECIFICATION WITH MARKINGS

In accordance with 37 C.F.R. § 1.121(b), Applicants submit a marked version of the specification, in order to indicate the changes Applicants have made to the specification.

IN THE SPECIFICATION:

This application is a continuation-in-part of the following Application Nos. filed on November 14, 2000: 60/274,622, 60/247,621, 60/247,620, 60/247,595, 60/247,594, 60/247,635, 60/247,634, 60/247,606, 60/247,607, 60/247,608, 60/247,609, 60/247,610, 60/247,611, 60/247,702, 60/247,701, 60/247,700, 60/247,699, 60/247,698, 60/247,807, 60/247,833, 60/247,832, 60/247,927, 60/247,926, 60/247,930, 60/247,929, 60/247,928, 60/247,797, 60/247,805, 60/247,804, 60/247,803, 60/247,802, 60/247,801, 60/247,800, 60/247,799, 60/247,798, 60/247,561, 60/247,560, 60/247,559, 60/247,558, 60/247,556, 60/247,612, 60/247,613, 60/247,614, 60/247,615, 60/247,616, 60/247,617, 60/247,633, 60/247,632, 60/247,631, 60/247,630, 60/247,629, 60/247,628, 60/247,627, 60/247,626, 60/247,625, 60/247,624, 60/247,806, 60/247,695, 60/247,794, 60/247,793, 60/247,792, 60/247,791, 60/247,790, 60/247,789, 60/247,788, 60/247,787, 60/247,786, 60/247,785, 60/247,784, 60/247,783, 60/247,782, 60/247,781, 60/247,780, 60/247,779, 60/247,778, 60/247,777, 60/247,776, 60/247,775, 60/247,774, 60/247,773, 60/247,772, 60/247,771, 60/247,770, 60/247,769, 60/247,768, 60/247,767, 60/247,766, 60/247,871, 60/247,872, 60/247,873, 60/247,874, 60/247,875, 60/247,981, 60/247,982, 60/247,983, 60/247,984, 60/247,745, 60/247,744, 60/247,743, 60/247,742, 60/247,623, 60/247,985, 60/247,840, 60/247,839, 60/247,838, 60/247,837, 60/247,836, 60/247,889, 60/247,890, 60/247,891, 60/247,892, 60/247,893, 60/247,741, 60/247,740, 60/247,739, 60/247,738, 60/247,737, 60/247,736, 60/247,735, 60/247,734, 60/247,733, 60/247,732, 60/247,731, 60/247,730, 60/247,728, 60/247,729, 60/247,727, 60/247,726, 60/247,761, 60/247,760, 60/247,759, 60/247,758, 60/247,757, 60/247,756, 60/247,765, 60/247,764, 60/247,763, 60/247,762, 60/247,755, 60/247,746, 60/247,725, 60/247,724, 60/247,723, 60/247,722, 60/247,721, 60/247,720, 60/247,719, 60/247,718, 60/247,717, 60/247,716, 60/247,754, 60/247,753, 60/247,752, 60/247,751, 60/247,750, 60/247,749, 60/247,748, 60/247,747, 60/247,796, 60/247,815, 60/247,814, 60/247,813, 60/247,812, 60/247,811, 60/247,810, 60/247,809,

60/247,808, 60/247,885, 60/247,884, 60/247,883, 60/247,882, 60/247,881, 60/247,880,
60/247,879, 60/247,878, 60/247,826, 60/247,835, 60/247,834, 60/247,897, 60/247,896,
60/247,895, 60/247,894, 60/247,901, 60/247,900, 60/247,899, 60/247,898, 60/247,903,
60/247,902, 60/247,919, 60/247,918, 60/247,917, 60/247,916, 60/247,915, 60/247,914,
60/247,913, 60/247,912, 60/247,911, 60/247,910, 60/247,877, 60/247,876, 60/247,707,
60/247,706, 60/247,705, 60/247,704, 60/247,703, 60/247,692, 60/247,691, 60/247,690,
60/247,689, 60/247,688, 60/247,687, 60/247,686, 60/247,685, 60/247,684, 60/247,683,
60/247,694, 60/247,693, 60/247,712, 60/247,711, 60/247,710, 60/247,709, 60/247,708,
60/247,697, 60/247,695, 60/247,565, 60/247,564, 60/247,545, 60/247,546, 60/247,547,
60/247,548, 60/247,568, 60/247,563, 60/247,570, 60/247,580, 60/247,555, 60/247,554,
60/247,553, 60/247,552, 60/247,551, 60/247,682, 60/247,681, 60/247,680, 60/247,679,
60/247,678, 60/247,677, 60/247,676, 60/247,655, 60/247,645, 60/247,795 and 60/247,656; and
this application is a continuation-in-part of the following Application Nos. filed on November
16, 2000: 60/248,607, 60/248,611, 60/248,609, 60/248,608, 60/248,606, 60/248,604,
60/248,603, 60/248,601, 60/248,600, 60/248,712, 60/248,711, 60/248,709, 60/248,708,
60/248,707, 60/248,706, 60/248,705, 60/248,704, 60/248,703, 60/248,702, 60/248,701,
60/248,700, 60/248,699, 60/248,698, 60/248,697, 60/248,696, 60/248,695, 60/248,694,
60/248,693, 60/248,692, 60/248,691, 60/248,690, 60/248,710, 60/248,689, 60/248,688,
60/248,687, 60/248,686, 60/248,720, 60/248,719, 60/248,718, 60/248,717, 60/248,716,
60/248,715, 60/248,714, 60/248,713, 60/248,536, 60/248,535, 60/248,733, 60/248,732,
60/248,731, 60/248,730, 60/248,729, 60/248,728, 60/248,727, 60/248,726, 60/248,725,
60/248,724, 60/248,723, 60/248,722, 60/248,721, 60/248,540, 60/248,539, 60/248,538,
60/248,537, 60/248,533, 60/248,532, 60/248,531, 60/248,530, 60/248,529, 60/248,528,
60/248,527, 60/248,526, 60/248,525, 60/248,524, 60/248,670, 60/248,789, 60/248,599,
60/248,745, 60/248,746, 60/248,747, 60/248,748, 60/248,744, 60/248,743, 60/248,756,
60/248,602, 60/248,598, 60/248,597, 60/248,596, 60/248,595, 60/248,594, 60/248,858,
60/248,857, 60/248,856, 60/248,855, 60/248,854, 60/248,853, 60/248,852, 60/248,851,
60/248,850, 60/248,849, 60/248,848, 60/248,792, 60/248,790, 60/248,669, 60/248,668,
60/248,667, 60/248,666, 60/248,665, 60/248,664, 60/248,793, 60/248,791, 60/248,684,
60/248,683, 60/248,682, 60/248,681, 60/248,680, 60/248,671, 60/248,679, 60/248,675,

60/248,676, 60/248,677, 60/248,678, 60/248,673, 60/248,674, 60/248,672, 60/248,784,
60/248,785, 60/248,786, 60/248,775, 60/248,773, 60/248,766, 60/248,765, 60/248,833,
60/248,783, 60/248,781, 60/248,780, 60/248,778, 60/248,767, 60/248,787, 60/248,774,
60/248,764, 60/248,782, 60/248,779, 60/248,685, 60/248,772, 60/248,771, 60/248,777,
60/248,776, 60/248,770, 60/248,768, 60/248,769, 60/248,796, 60/248,797, 60/248,795,
60/248,794, 60/248,663, 60/248,662, 60/248,660, 60/248,659, 60/248,658, 60/248,656,
60/248,654, 60/248,653, 60/248,651, 60/248,650, 60/248,648, 60/248,647, 60/248,645,
60/248,643, 60/248,642, 60/248,640, 60/248,637, 60/248,636, 60/248,634, 60/248,632,
60/248,631, 60/248,630, 60/248,629, 60/248,627, 60/248,625, 60/248,763, 60/248,761,
60/248,759, 60/248,757, 60/248,754, 60/248,753, 60/248,749, 60/248,616, 60/248,615,
60/248,614, 60/248,613, 60/248,612, 60/248,605, 60/248,610, 60/248,661, 60/248,657,
60/248,655, 60/248,652, 60/248,649, 60/248,646, 60/248,644, 60/248,641, 60/248,639,
60/248,638, 60/248,635, 60/248,633, 60/248,628, 60/248,626, 60/248,624, 60/248,762,
60/248,760, 60/248,758, 60/248,755, 60/248,752, 60/248,751, 60/248,750, 60/248,742,
60/248,741, 60/248,740, 60/248,739, 60/248,736, 60/248,735, 60/248,734, 60/248,623,
60/248,622, 60/248,621, 60/248,738, 60/248,737, 60/248,620, 60/248,619, 60/248,618, and
60/248,617.

BACKGROUND OF THE INVENTION

(i) Field of the Invention

The present invention relates to a therapeutic composition comprising at least one antigen, in particular an antigen of viral, bacterial or parasitic origin, or at least one in vivo generator of a compound comprising an amino acid sequence, and at least one adjuvant.

(ii) Description of Related Art

The use of adjuvants in therapeutic compositions of the vaccine type has been known for a long time. The main objective of these adjuvants is to allow an increase in the immune response. These adjuvants are diverse in nature. They may, for example, consist of liposomes, oily phases, for example the Freund type of adjuvants, generally used in the form of an emulsion with an aqueous phase, or, more commonly, may consist of water insoluble inorganic salts. These inorganic salts may consist, for example, of aluminum hydroxide, zinc sulfate, colloidal iron hydroxide, calcium phosphate or calcium chloride. Aluminum hydroxide ($\text{Al}(\text{OH})_3$) is the

most commonly used adjuvant. These adjuvants are described in particular in the article by Rajesh K. Gupta et al "Adjuvants, balance between toxicity and adjuvanticity", Vaccine, Vol. 11, issue 3, 1993, pages 993-306.

The adjuvants mentioned above have the drawback of limited efficiency. Moreover, they may include a certain toxicity with regard to individuals treated. More particularly, when these therapeutic compositions are injected, the formation of lesions and other local reactions such as granulomae is observed at the point of injection. These drawbacks are less pronounced